

Medical Countermeasures for Radiation Combined Injury:

Radiation with Burn, Blast, Trauma and / or Sepsis

March 26 – 27, 2007

**Embassy Suites Hotel
Chevy Chase, MD**



Meeting Objectives

- **Characterize Features of, and Identify Research Priorities that Need to be Addressed for Radiation Combined Injury:**
 - Radiation + Sepsis
 - Radiation + Burn
 - Radiation + Wound
- **Animal Models**
- **Endpoints to be Studied**
- **Countermeasures for Combined Injury**
 - Currently Available?
 - Future Directions?

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Animal Rule: Summary

- Mechanism of action of the drug is known
- Mechanism of pathogenesis of combined injury in both animal and man is known (and know that they are similar)
- Drug metabolism (PK, PD, TK) in animal and man are known, and can be reliably scaled
- Two species: Not always required
- Phase 1 human safety studies

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Animal Models

- **Validated Models - Species Considerations**
 - **Small Animals (Mouse, Rat)**
 - **Large Animals (Swine, Canine, Non-Human Primate)**
- **General Parameters**
 - **Supportive Care (Fluids, Antibiotics, Analgesics, Anti-Pyretics)**
 - **Length of Time to Follow Animals**
- **IACUC Considerations**
 - **Euthanasia Criteria**
- **Statistical Considerations**

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Endpoints

- **Common Endpoints**
 - **Mortality**
 - DMF
 - Acceptable Surrogates?
 - **Hematological Parameters**
 - **Cytokine Arrays (Other Indicators?)**
- **Model-Specific Endpoints**
 - **Bacterial Load**
 - **Burn Healing**
 - **Reduction in Wound Size**
 - **Cognitive Tests**

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Countermeasure Development (1)

- **Physiological Challenges Unique to Combined Injury**
 - **Multi-Organ Involvement**
 - **Anti-Microbials**
 - **Wound Healing**
 - **Modulation of Inflammatory Response**
 - **Medical Management**
 - **Others?**

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Countermeasure Development (2)

■ Regulatory Challenges

- Validated Animal Model
- Mechanisms of Combined Injury
- Mechanisms of Action of Countermeasures

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Radiation Factors

- Dose (LD 50 or Lower)
- Radiation Quality
 - Gamma
 - Mixed Field



Combined Injuries

- **Sepsis**
 - Preferred Microbe for Animal Studies
 - Methods of Microbe Exposure
- **Blast/Wound**
 - Types of Wounds Possible
 - Open
 - CNS / Head Trauma
 - Lung Blast Injury
 - Crush Injury
 - Methods to Create Wounds
- **Burn**
 - Types of Burn Expected
 - Radiation (Gamma, Beta)
 - Thermal
 - Partial- vs. Full-Thickness
 - Methods to Create Burn

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